REMARKS

Status of the Claims

Claims 1-12 are pending and claims 1-4 are under consideration in this application. Claims 1 and 3 are cancelled without prejudice or disclaimer. Claims 2, 4, 5, 6, 7, 9, 10, and 12 are amended. The title and the Abstract of the specification have also been amended. Support for the amendments made herein can be found in the specification at, e.g., page 8, paragraph 3 and page 20 to 21. No new matter is added.

Following entry of the amendments and cancellations made herein, claims 2 and 4-12 will be pending and claims 2 and 4 will be under consideration in this application.

Objections to the Specification

(i) At page 3 of the Office Action, the specification is objected to because the title is allegedly not descriptive of the claims. The title, as amended, reads: "Novel glycerol kinase, which has high resistance against preservative." As acknowledged by the Office Action, such an amendment renders the objection moot.

(ii) At page 3 of the Office Action, the Abstract is objected to for allegedly not completely describing the disclosed subject matter. Applicants have herein amended the first paragraph of the Abstract to read: "The disclosure relates to (i) a gene isolated from *Cellulomonas sp.* JCM2471, the gene encoding a new glycerol kinase and (ii) a method for preparing the glycerol kinase by gene recombination technique." As acknowledged by the Office Action, such an amendment renders the objection moot.

Rejections Under 35 U.S.C. §112, second paragraph (Indefiniteness)

At pages 3 and 4 of the Office Action, claims 1-4 are rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite.

Claim 1 has been cancelled, thereby obviating its rejection.

The Office Action states that "Claim 2 (Claim 3 dependent therefrom) recites the limitation 'remaining ratio is 70% or more', which is a relative term." (See Office Action at page 4). While not conceding to any aspect of the Examiner's stated reasons for rejection, claim 2 has been amended to recite, *inter alia*, "at least 70% or more of the kinase activity of the protein is retained when the protein is incubated for one week at 25°C in the presence of 100 mg/L of N-methylisothiazolone or derivatives thereof.

In view of the amendments and cancellations made herein, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Rejection Under 35 U.S.C. §112, first paragraph (Written Description)

At pages 4 to 6 of the Office Action, claims 1-4 are rejected under 35 U.S.C. §112, first paragraph as allegedly lacking written description. According to the Office Action,

> instant claims 1-4 are drawn to a glycerol kinase which has high resistance against preservative.
> ....
> the instant specification and the prior art cannot describe the structure of a very broad claimed genus and one skilled in the art would not be in possession of the claimed genus of glycerol kinase by the instant specification." (See Office Action at page 5, lines 4 and 5 and page 6, lines 17-20).

Applicants submit the following remarks to show that the instant claims are fully supported by the disclosure such that one of ordinary skill in the art would believe the Applicants in full possession of the claimed genus of isolated proteins.

According to the MPEP,

> [t]he written description for a claimed genus may be satisfied through sufficient description of a representative number of species by…disclosure of relevant, identifying characteristics, i.e., **structure or other physical and/or chemical properties**, by functional characteristics coupled with a known or disclosed correction between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus[.] (Emphasis added; see MPEP §2163 citing *Eli Lilly*, 119 F. 3d at 1568, 43 USPQ2d at 1406).

Claims 1 and 3 are cancelled thereby rendering their rejection moot.

Claim 2, as amended, is drawn to an isolated protein that has glycerol kinase activity. The claimed protein is required to have a number of physical and chemical properties that include: (1) the activity of the protein has the ability to modify glycerol, in the presence of ATP, to glycerol-3-phosphoric acid; (2) the activity of the protein is optimal at a pH of about 10.0; (3) the activity of the protein is optimal at a temperature of about 50°C, wherein the reaction is carried out for five minutes in the presence of 20 mM HEPES buffer at a pH of about 7.9; (4) at least 90% or more of the activity of the protein is retained after incubation of the protein at 25°C for two hours at a pH of about 6.0 to about 10.0; (5) at least 90% or more of the activity of the protein is retained after incubation of the protein for about 15 minutes in 50 mM potassium phosphate buffer at a pH of about 7.5; (6) the protein contains a subunit that has a molecular weight of about 55,000 daltons as determined by sodium-dodecyl sulfate polyacrylamide gel electrophoresis or the intact protein has a molecular weight of about 176,000 daltons as determined by gel filtration; (7) the glycerol kinase activity has a K_m of about 6.9 x 10^{-6} M for glycerol and a K_m of about 1.11 x10^{-4} M for ATP; (8) the protein has a relative activity of about 41.2 Units/mg; and (9) at least 70% or more of the kinase activity of the protein is retained when the protein is incubated for one week at 25°C in the presence of 100 mg/L of N-methylisothiazolone or derivatives thereof. As such, the genus of isolated proteins embraced by the claims does not have substantial variation, since all of the proteins must not only have glycerol kinase activity, but also each of the physical and chemical properties recited above including, e.g., a specified molecular weight. In this way, all members of the genus of isolated proteins are highly similar in functional, physical, and chemical properties; and methods for determining whether an isolated protein has, e.g., a glycerol kinase activity or any of the physical and chemical properties recited in the claims are provided in the specification and known in the art. Nothing more is required under the law.

Claim 4, which incorporates all of the limitations of claim 2, further specifies the structure of the protein such that the protein must consist of an amino acid sequence represented by SEQ ID NO:1 in the Sequence Listing or comprise the amino acid sequence depicted in SEQ

ID NO:1, wherein one or several amino acids are deleted, substituted or added and having glycerol kinase activity.

Therefore, in light of the disclosure contained in the application as filed, the skilled artisan would have concluded that the inventors were in possession (at the time of filing of the present application) of the necessary common attributes possessed by the members of the claimed genus.

The Office Action cited *Regents of the University of California v. Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997), a leading case on the written description requirement for nucleic acid molecules, in support of the present rejection. The discussion in *Lilly* regarding a proper written description for genus claims had to do with a claim drawn to a vertebrate mRNA encoding insulin. The *Lilly* court held that a generic statement, such as the term "mammalian insulin cDNA" is not, without more, an adequate written description of an invention claiming the nucleotide sequence for human insulin. The court's decision in *Lilly* focused on functional claims directed merely to a desired result without structure: "[t]he description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention." *Id.* at 1406. However, the *Lilly* court also took care to indicate that structural information about the claimed genus was different in kind than a mere desired result. The court indicated that in claims involving chemical materials such as proteins and polynucleotides "generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is usually an adequate description of the claimed genus." *Id.*

As described above, instant claim 2 is drawn to an isolated protein that is defined by a number of physical and chemical properties, such as molecular weight. Moreover, the claimed invention is also defined by the recited function of the protein (i.e., the glycerol kinase activity). The claim is not directed to a mere desired result without structure, as was the case in *Lilly*. A person of ordinary skill in the art would clearly understand the physical and chemical definition of the isolated protein provided by claim 2 and 4, and would therefore understand the inventors

to have been in possession of the claimed protein at the time the application was filed. Accordingly, claims 2 and 4 satisfy the written description requirement. Applicants respectfully request reconsideration and withdrawal of the written description rejection.

Rejection Under 35 U.S.C. §112, first paragraph (Enablement)

At pages 6 to 9 of the Office Action, claims 1-4 are rejected under 35 U.S.C. §112, first paragraph as allegedly lacking enablement. According to the Office Action, "the specification, while being enabling for glycerol kinase consisting of SEQ ID NO:1 from Cellulomonas sp. JCM2471, does not reasonably provide enablement for **any** glycerol kinase having a resistance against preservative." (Emphasis added; see Office Action at page 7).

Applicants respectfully submit that the instant claims are enabled such that one of ordinary skill in the art could make and use the claimed isolated proteins with little more than routine experimentation.

The claimed invention is based, at least in part, on the isolation (from a *Cellulomonas sp.* JCM2471 bacterium) of a gene encoding a glycerol kinase having the amino acid and nucleotide sequences depicted in SEQ ID NO:2. The isolated glycerol kinase was tested extensively and found to have a number of chemical and physical properties including those recited in the claims. (See instant claim 2 and 4 and the specification at, e.g., page 8 and pages 25 to 41 (Working Examples 1 to 6)). Furthermore, as noted above, the specification provides the methods used to determine the amino acid sequence of (and the nucleic acid encoding) the isolated protein and that the protein had a glycerol kinase activity and the above-mentioned physical and chemical properties. (See specification at, e.g., pages 21 to 24, and the Working Examples 1-6, at pages 25 to 41). Such methods would allow the skilled artisan to make and use not only the glycerol kinase identified by the inventors, but any proteins within the scope of claims 2 and 4 with little more than routine experimentation. That is, it is well within the capability of a skilled artisan to prepare an isolated protein that has, e.g., a molecular weight as specified by the claims (i.e., the protein contains a subunit that has a molecular weight of about 55,000 daltons as determined by sodium-dodecyl sulfate polyacrylamide gel electrophoresis or the protein has a molecular weight

of about 176,000 daltons as determined by gel filtration). It is also within the artisan's skill to prepare an isolated protein that has the amino acid sequence of SEQ ID NO:1 with or without one or several amino acids deleted, substituted or added. For example, standard mutagenesis techniques can be used produce variants of SEQ ID NO:1 and examples of such methods are provided in the specification.

In light of the foregoing remarks, applicants respectfully submit that one of ordinary skill in the art would have been able, at the time of filing of the present application, to make and use the claimed polypeptides without undue experimentation and with a reasonable expectation of success. Accordingly, Applicants request reconsideration and withdrawal of the enablement rejection.

Rejection Under 35 U.S.C. §101 (Non-statutory Subject Matter)

At page 9 of the Office Action, claims 1-4 are rejected under 35 U.S.C. §101 as allegedly drawn to non-statutory subject matter.

While not conceding to any aspect of the Examiner's stated reason for rejection, the claims, as amended, are drawn to "isolated" proteins, which do not occur in nature. Accordingly, the rejection is moot.

Rejection Under 35 U.S.C. §102(b) (Anticipation)

At page 10 of the Office Action, claims 1-4 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Wilkison et al. (J. Biol. Chem. (1991) 266:16886-16891).

According to the Office Action,

> Wilkison et al. teach a glycerol kinase from "Cellulomonas sp." ... The kinase of Wilkison et al. would have the same amino acid sequence as the instant SEQ ID NO:1 ... thus the glycerol kinase of Wilkison et al. also would have same resistancy against the disclosed concentration ... of preservative methylisothiazolone compared to the instant glycerol kinase. (See Office Action at page 10).

From this, Applicants understand the Examiner's position to be that the glycerol kinase of Wilkison et al. inherently anticipates the claimed isolated proteins. Applicants respectfully disagree with this characterization in view of the following remarks.

According to the MPEP, to establish a *prima facie* case of inherent anticipation "the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." (Emphasis in the original; see MPEP § 2112, citing *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." (See MPEP § 2112, citing *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)). "The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." (See MPEP §2112, citing *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993)).

Claims 1 and 3 are cancelled thereby rendering their rejection moot. Instant claims 2 and 4 are discussed above.

Wilkison et al. discloses, *inter alia*, that a glycerol kinase "isolated from *Cellulomonas sp.* was able to phosphorylate monobutyrin." (See Wilkison et al. at page 16887, column 2). However, Wilkison et al., as cited by the Office Action, does not disclose or even suggest that the glycerol kinase exhibited any of the chemical or physical properties, let alone all of the properties, required by claim 2. Particularly, Wilkison et al. does not disclose that the glycerol kinase has a molecular weight of approximately the protein contains a subunit that has a molecular weight of about 55,000 daltons (as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis) nor that the intact protein has a molecular weight of about 175,000 daltons (as determined by gel filtration). Furthermore, Wilkison et al. tested the ability of the kinase to phosphorylate monobutyrin, not the ability to modify glycerol, in the presence of ATP, to glycerol-3-phosphoric acid, and certainly did not test if the kinase has a K_m of about 6.9 x 10^{-6} M for glycerol and a K_m of about 1.11 x10^{-4} M for ATP. Moreover, Wilkison et al. does

not disclose or even suggest that the glycerol kinase consists of the amino acid sequence depicted in SEQ ID NO:1 (or comprises the amino acid sequence of SEQ ID NO:1, wherein one or several amino acids are deleted, substituted or added) as required by claim 4.

In the experimental procedures, the authors of the Wilkison et al. reference state that "[g]lycerol kinases were purchased from Sigma." (See Wilkison et al. at page 16886, column 1). Applicants believe that the authors are referring to Sigma Aldrich having a place of business in St. Louis, MO. However, like Wilkison et al., Sigma does not disclose or even suggest that the glycerol kinase exhibited any of the properties required by claim 1; nor that the kinase has an amino acid sequence of SEQ ID NO:1, and certainly not that the kinase was isolated from *Cellulomonas sp.* JM2471. (See Sigma's product website: http://www.sigmaaldrich.com/catalog/search/ProductDetail/SIGMA/G6142).

Therefore, the only disclosed characteristics of Wilkison et al.'s glycerol kinase are that it (a) is isolated from a *Cellulomonas sp.* bacterium and (b) has the ability to phosphorylate monobutyrin. There is no evidence of record that would lead a skilled artisan to conclude that the "glycerol kinase" of Wilkison et al. necessarily has each and every one of the physical and chemical requirements of claim 2 or the specific amino acid sequences required by claim 4. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102.

CONCLUSION

For the reasons set forth above, Applicants submit that all grounds for objection and rejection have been overcome and that all of the pending claims are now in condition for allowance, which action is earnestly requested. Applicants do not accede to any positions of the Examiner not specifically addressed above.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at the number provided below.

No fees are believed to be due. However, please apply any charges or credits to deposit account 06-1050, referencing Attorney Docket No. 18965-002US1.

Respectfully submitted,

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